

# **NEUROFIT** SAS

Pre-Clinical CRO  
CNS & PNS preclinical Services

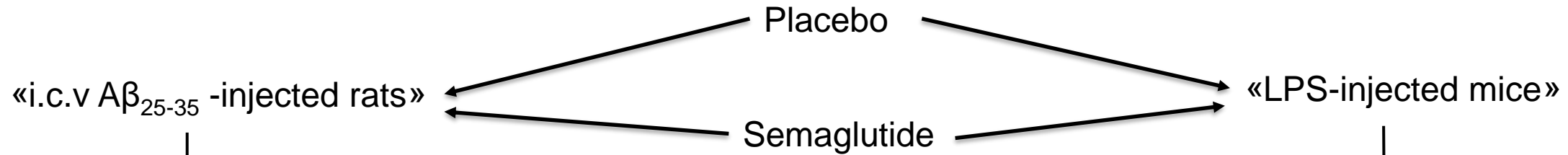
## Semaglutide's cognitive rescue: insights from rat and mouse models of Alzheimer's disease

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# Introduction / Objective

- **Semaglutide is a drug from the Glucagon-like peptide-1 (GLP-1) class that promotes weight loss and improves hyperglycemia.**
- **GLP-1 drugs appear to affect multiple aspects of the metabolic system implicated in Alzheimer's disease, including amyloid and inflammation pathways.**
- **The present study investigates the impact of Semaglutide treatment on:**
  - **in-vivo amyloid- $\beta$  ( $A\beta$ ) -induced memory deficit in the rats**
  - **in-vivo inflammation (LPS) -induced cognitive deficit in mice**
  - **in-vitro brain inflammation (LPS) -induced neuronal death in glia-neuron coculture system**

# In-vivo experimental protocol



### PASSIVE AVOIDANCE PARADIGM

The diagram illustrates the passive avoidance paradigm. A mouse is shown on a bridge between two compartments. The left compartment is labeled 'Black dark compartment' and contains a lightbulb icon. The right compartment contains a mouse receiving a 'Mild foot shock' (indicated by a lightning bolt). A 'Correct response' is shown as the mouse avoids the dark compartment, while a 'Punished response' is shown as the mouse enters the dark compartment. A stopwatch icon is also present.

Memory performance is positively correlated with the latency to leave the bridge and avoid the adverse stimulus, thus the better the recollection, the greater the "step through latency".

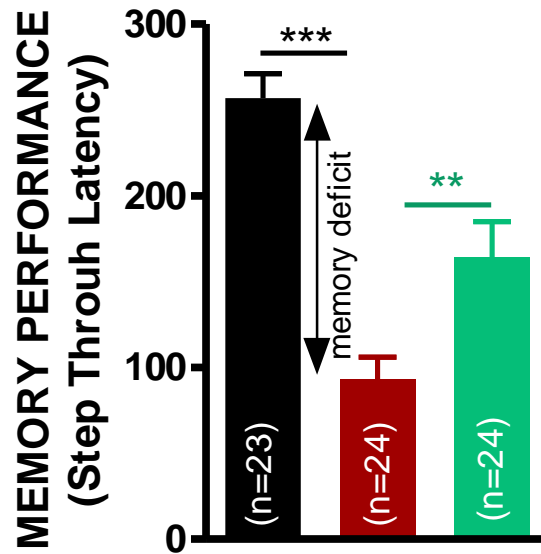
### T-MAZE ALTERNATION PARADIGM

The diagram shows a T-maze with a mouse at the start. The two arms are labeled 'Left' and 'Right'. A question mark is above the mouse, indicating a choice. The mouse is shown moving into the right arm.

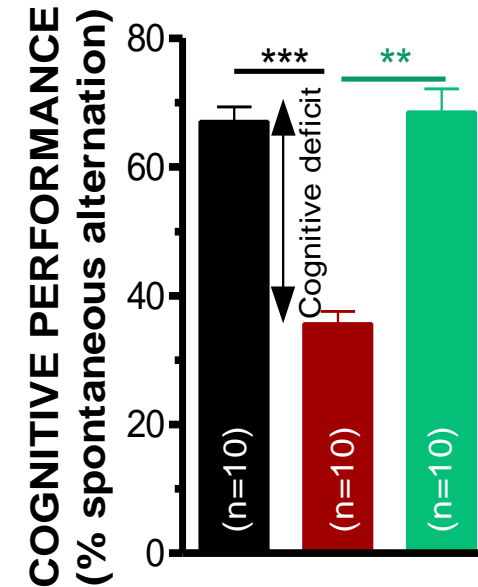
The lower the percentage of alternation between the left and right arms of the T-maze, the poorer the cognitive performance of the mice

# Impact of Semaglutide treatment on rodents with memory and cognitive deficit

■ Sham / Vehicle  
■ i.c.v. A $\beta$  / Vehicle  
■ i.c.v. A $\beta$  / Semaglutide (0.1 mg/kg)



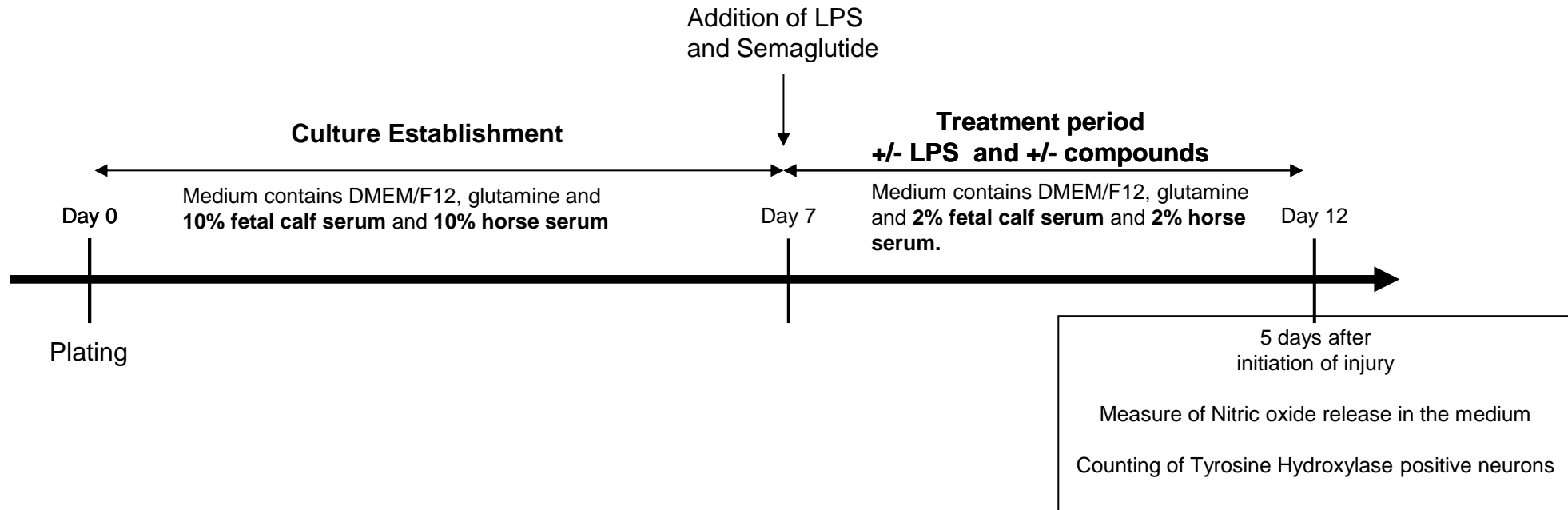
■ Saline / Saline  
■ LPS 250  $\mu$ g/kg / Saline  
■ LPS 250  $\mu$ g/kg / Semaglutide (0.1mg/kg)



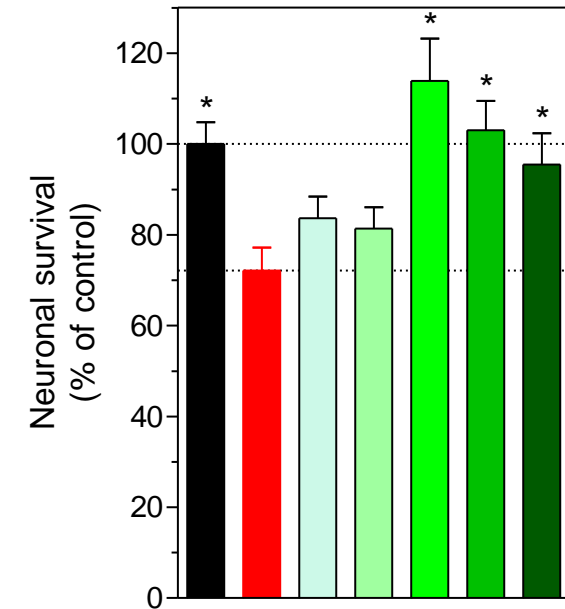
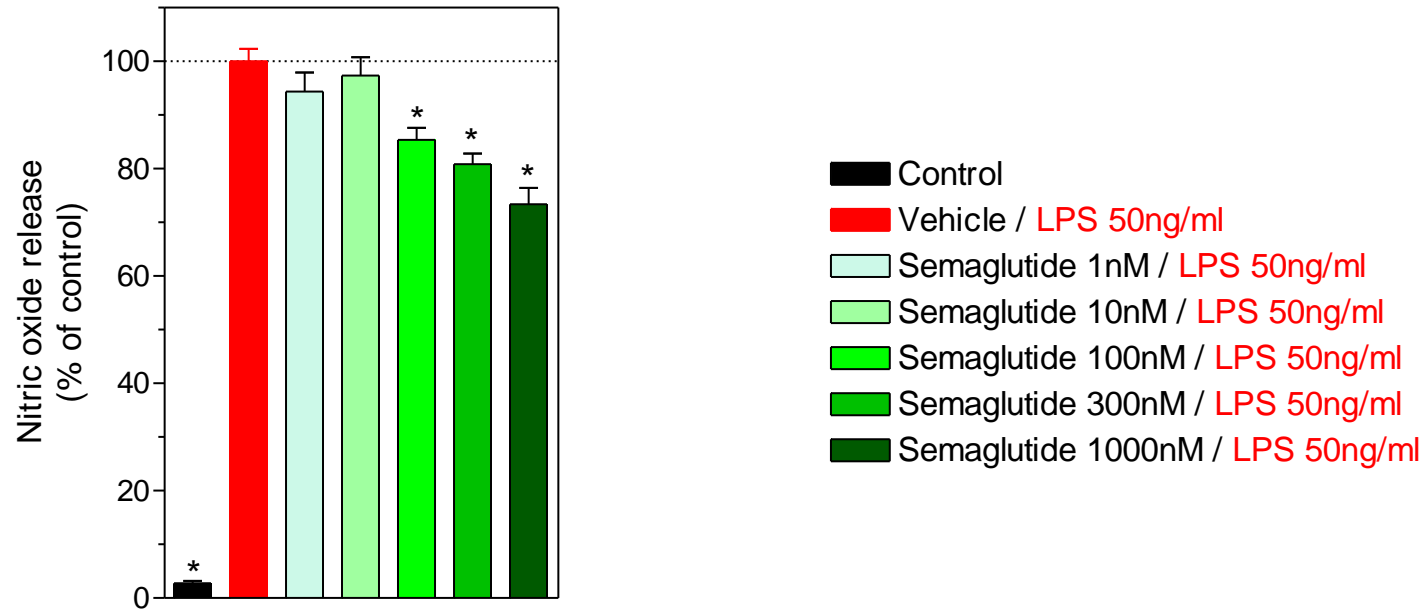
⇒ One week Semaglutide significantly improves the memory deficit in rats i.c.v. A $\beta$  injections.

⇒ One week Semaglutide fully restores the cognitive deficit of LPS-treated mice, suggesting a potential anti-inflammatory effect.

# Primary neuronal culture experimental protocol



# Impact of Semaglutide treatment on Neuronal death and nitric oxide release induced by LPS in glia-neuron coculture



⇒ Dose-response inhibition of nitric oxide release by Semaglutide in glia-neuron co-cultures, which suggests a potential anti-inflammatory action Semaglutide.

⇒ Dose-response inhibition of LPS-induced neuronal death by Semaglutide in glia-neuron co-cultures, most probably via its anti-inflammatory action.



# Conclusion

- These results support the beneficial effect of Semaglutide treatment against amyloid- $\beta$  -induced cognitive deficit.
- They also indicate that an anti-inflammatory effect of Semaglutide could be one of the primary mechanisms behind this benefit.

